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Cerebral Palsy and Autism Associated With Periventricular White Matter Hyperintensity on Brain Magnetic Resonance Imaging: A New Disorder and Its Treatment

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Research Article

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Abstract

Background: We have previously reported the very rare sporadic occurrence of periventricular white matter hyperintensity on brain magnetic resonance imaging with atypical neuropsychiatric manifestation including late onset (after the first year) non–progressive spastic cerebral palsy, and autistic features. There is no published experience with treatment with such rare conditions.

Patients and methods: A Palestinian boy from the Western Bank who had a diagnosis of cerebral palsy (mild spastic diplegia) and gross sensory motor delay with development of autistic features was previously reported to have a very rare condition consisting of spastic cerebral palsy and autism associated with periventricular white matter hyperintensity on brain magnetic resonance imaging.

Results: Before treatment, at the about the age of five year and half year, he was unable to stand from sitting position on the floor alone, but he could walk very slowly for few steps, but was falling on his head several times. He was not saying any word and had impaired communication with others as he was not responding to his name most of the time. The boy was treated with courses of multi–factorial therapies based on our extensive published experiences with the treatment of cerebral palsy and autism.

After four months of treatment, the boy showed significant improvement in motor abilities and he was able to stand from the sitting position on the floor alone, and he was walking confidently for long time and also going upstairs holding the bars. Autistic features improved and he was much more responsive to his name than before treatment, and his eye contact was better. His communication skills improved and was increasingly asking to go out and waving goodbye.

Conclusion: In this paper the emergence of a new clinical disorder is emphasized. It is characterized by the association of cerebral palsy and autism with periventricular white matter hyperintensity on brain magnetic resonance imaging. Treatment of the disorder with courses of evidence–based multi–factorial was associated with significant improvement.

Keywords: Periventricular White Matter Hyperintensity; Cerebral Palsy; Autism; Multi–Factorial Therapies.

Introduction

Periventricular leukomalacia is the most common abnormalities seen in children with cerebral palsy especially of the spastic type. However, the association of cerebral palsy with imaging study showing findings similar to the findings of leukodystrophy have been reported [1–3].

In 1996 Kristjánsdóttir et al from Sweden studied 78 pediatric patients with white matter abnormalities on magnetic resonance imaging, 13 patients with an apparently leukodystrophic white matter had non–progressive poorly defined non–specific disorders [4].

Autistic disorders are heterogeneous and very complex group of chronic disorders that are associated with marked early impairment in socialization and communication. The association

of autism disorders with significant brain imaging abnormalities has been infrequently reported. However, we have previously reported that brain imaging abnormalities in patients with autism disorders include arachnoid cyst, agenesis of the corpus callosum, evidence of vasculitis (In Heller syndrome), and brain imaging abnormalities related to a coexisting condition such as cerebral palsy [5].

We have previously reported the very rare sporadic occurrence of periventricular white matter hyperintensity on brain magnetic resonance imaging with atypical neuropsychiatric manifestation including late onset (after the first year) non–progressive spastic cerebral palsy, and autistic features. There is no published experience with treatment with such rare conditions [6].

Patients and methods

A Palestinian boy from the Western Bank who had a diagnosis of cerebral palsy (mild spastic diplegia) and gross sensory motor delay with development of autistic features was previously reported to have a very rare condition consisting of spastic cerebral palsy and autism associated with periventricular white matter hyperintensity on brain magnetic resonance imaging.

The patient was born prematurely on 7th of November 2016 at 32 weeks gestation by an emergency cesarean section. He was a result of in vitro fertilization pregnancy, and was the 3rd between his siblings. His Apgar score at birth was 9 at 0 second, but he was intubated 9 hours after delivery due to acute respiratory distress syndrome and remained in the intensive care unit for 19 days. On the third day of delivery, he was hypotonic, but his tone improved thereafter. When he discharged from hospital, he did not have apparent complications, and repeated investigations showed normal findings.

The boy was fed both breast and bottle during infancy. His growth and development was regarded acceptable until the age of 18 months, when he received MMR vaccination, within 10 hours, he became very sick and developed severe flu–like symptoms and lethargy. He lost 3 kg in one week. Thereafter, he started to regress and became mute and started to display autistic features.

Family history was negative for a similar condition despite that all of his siblings were born prematurely, but without developing complications or neurological abnormality.

The boy had a 20–year old sister, 17–year old sister who was born at 27th week of gestation, but she was totally doing well and was great, and a younger 2–year old healthy brother.

At the age of two years, brain MRI revealed bilateral periventricular zones of white matter hyperintensity on the FLAIR and T2 weighted images appearing hypointense on T1 weighted images, more prominent at the posterior aspect of the lateral periventricular regions. The subcortical white matter, the basal ganglia, thalamus, the corpus callosum, the brainstem and cerebellum all had normal appearance. MRI also showed cavum septum pellucidum with cavum vergae which is a common anatomical variant.

The boy had leukodystrophy like picture with bilateral periventricular zones of increased signal intensity on T2 and FLAIR MRI images. The MRI report emphasized that a delayed myelination is less likely.

He was treated with vitamin D, l–carnosine, omega 3, phosphatidylcholine syrup, hyperbaric oxygen therapy, and physiotherapy, but without obvious response.

Results

Before treatment, at the about the age of five year and half year, he was unable to stand from sitting position on the floor alone, but he could walk very slowly for few steps, but was falling on his head several times.

He was not saying any word and had impaired communication with others as he was not responding to his name most of the time. He was laughing out loud out of a sudden with no apparent reason. He was sometimes looking at his hand while waving with it. He was refusing solid food and accepting some soft pure food especially yogurt with jam, and was preferring sweetie foods.

The boy was treated with courses of multi–factorial therapies (Table–1) based on our extensive published experiences with the treatment of cerebral palsy and autism [7–17]. Treatment courses included intramuscular cerebrolysin, oral citicoline, oral piracetam, and oral muscle relaxant including baclofen and diazepam, and intramuscular nandrolone decanoate. Nutritional support was provided mainly in the form of Royal–plus soft gel capsules (Divided and given with little juice or milk in the morning and at 5 pm) which contains royal jelly and omega–3, and amino acid supplementation.

Table–1: The courses of multi–factorial therapies.

The Courses Of Multi–Factorial Therapies
First Two Month Course
Intramuscular cerebrolysin: 3ml given every third day during the day, preferably in morning (20 doses over 2 months). **Oral baclofen**: 5 mg twice daily, increased to 3 times daily during the second month. **Oral citicoline:** 300 mg once daily in the morning. **Intramuscular nandrolone decanoate:** 12.5 mg initially and second dose after an interval of 2 weeks. **Oral diazepam:** 2 mg daily at night (Added after one month of treatment.
Second Two Month Course
Intramuscular cerebrolysin: 4ml given every third day during the day, preferably in morning (20 doses over 2 months). **Oral baclofen**: 5mg twice daily, increased to 3 times daily during the second month. **Oral citicoline:** 3 mg once daily in the morning. **Intramuscular nandrolone decanoate:** 12.5 mg (One dose). **Oral piracetam:** 800 mg in the morning.

After four months of treatment, the boy showed significant improvement in motor abilities and he was able to stand from the sitting position on the floor alone, and he was walking confidently for long time and also going upstairs holding the bars. Autistic features improved and he was much more responsive to his name than before treatment, and his eye contact was better. His communication skills improved and was increasingly asking to go out and waving goodbye.

In addition, he developed interest in games and toys suggesting some cognitive improvement.

Discussion

In 2000, Kristjánsdóttir, Uvebrant, and Wiklund from Sweden described fifteen pediatric patients who had non–specific clinical neurological had leukodystrophy–like white matter abnormalities on brain MRI, and had non–progressive clinical manifestations and course.

The patients of Kristjánsdóttir and colleagues had early onset of symptoms within the first year of life, most often presenting as general developmental delay and hypotonia. Later appearing signs were spasticity and ataxia and as a rule severe learning and motor disabilities. Serious ocular abnormalities were frequent [18].

The patient in this paper had autistic features (Poor response to name, poor eye contact, and poor speech) plus clinical and imaging evidence of cerebral palsy, therefore courses of intramuscular cerebrolysin were used because cerebrolysin is the only medication that is associated with cure of the major autistic features (Poor response to name, and poor eye contact). In addition, cerebrolysin has been used extensively as a part of cerebral palsy multi–factorial therapies for its brain repairing properties [7–17].

Cerebrolysin solution contains free amino acids (85%) and 15% biologically active low molecular weight amino acids including neuro–peptides (Brain–derived neurotrophic factor, glial cell line–derived neurotrophic factor, nerve growth factor, ciliary neurotrophic factor . Cerebrolysin has been used safely with benefit in a variety of neuro–psychiatric disorders including idiopathic mental retardation, cerebral palsy, myelomeningocele, pediatric juvenile spinal muscular atrophy, pediatric Charcot Marie Tooth disease, kernicterus, agenesis of corpus callosum with colpocephaly [11,13,19–26].

The boy's difficulty in walking was attributed to important extent to spasticity, therefore, baclofen was given in a relatively small dose of 5mg twice daily based on our extensive published experiences with the treatment of spastic cerebral palsy [3,8,13–15].

Citicoline was used in this patient because of its usefulness in the treatment of autism as it can stimulate and improve speech, and also because it has been used extensively as a part of cerebral palsy multi–factorial therapies of cerebral palsy [7–17].

Citicoline, which has been increasingly grouped with the water soluble B vitamins, and is regarded as a form of the essential nutrient choline. It has been increasingly used with noticeable benefits in the treatment of several pediatric neuro–psychiatric disorders including, pervasive developmental disorders including Rett syndrome, and kernicterus [7, 9, 11, 25, 27].

Low dose intramuscular nandrolone decanoate for its beneficial muscle strengthening effect and its reported usefulness in cerebral palsy [3,15].

Piracetam was added for its beneficial role in developmental retardation [20,21], and because it has been used extensively as a part of cerebral palsy multi–factorial therapies of cerebral palsy [7–17].

Piracetam beneficial effects on impaired cerebral functions include improving neuronal and cognitive functions, increasing cerebral blood flow and oxygen consumption, improving neurotransmitters function and brain neurotransmission. Piracetam is not associated with important side effect nor has acute toxicity at the therapeutic doses. Piracetam has been used with important benefits in the treatment of cerebral palsy and other childhood neuro–psychiatric disorders [28–30].

Conclusion

In this paper the emergence of a new clinical disorder is emphasized. It is characterized by the association of cerebral palsy and autism with periventricular white matter hyperintensity on brain magnetic resonance imaging. Treatment of the disorder with courses of evidence–based multi–factorial was associated with significant improvement.

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None.

Conflict of interest

None.

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